REMARKS

Reconsideration is requested.

Claims 26-59 are pending. Claims 54-59 have been added and find support throughout the specification, such as in the first paragraph on page 4 of the application. No new matter has been added.

The allowance of claims 27, 28, 30, 34, 35, 37, 41, 42, 44, 48, 49 and 51 is acknowledged, with appreciation. See, page 1 of the Office Action dated October 1, 2003 (Paper No.5).

The specification has been amended above in response to the Examiner's comment on page 2 of Paper No. 5. Entry of the above amendment is requested to correct the inadvertent error introduced in the Amendment dated January 15, 2002.

The Section 102 rejection of claims 26, 29, 31, 32, 47, 50, 52 and 53 over Houghton (EP 0388232), is traversed. Reconsideration and withdrawal of the rejection are requested as Houghton fails to teach each and every aspect of the presently claimed invention. Specifically, the invention of the rejected claims recite sequences not specifically described in Houghton. Withdrawal of the Section 102 rejection is requested.

The Section 103 rejection of claims 33, 36, 38, 39, 40, 43, 45 and 46 over Houghton is traversed. Reconsideration and withdrawal of the rejection are requested as, at best, Houghton may have provided one of ordinary skill in the art an invitation to conduct further experimentation however such an invitation is not sufficient to establish a *prima facie* case of obviousness but rather can, at best , establish that it may have been obvious to try to make the presently claimed invention. The Section 103 rejection

of the noted claims over Houghton should be withdrawn. As further evidence of the patentability of the claimed invention, the Examiner is requested to see the evidence in the attached Annex 1 wherein the peptides of the present invention are demonstrated as being superior as compared to the specific peptides of Houghton. Reconsideration and withdrawal of the Section 103 rejection of the noted claims over Houghton is requested.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested. The Examiner is requested to contact the undersigned if anything further is required in this regard.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: _____
B. J. Sadoff
Reg. No. 36,663

BJS:plb
1100 North Glebe Road, 8th Floor
Arlington, VA 22201-4714
Telephone: (703) 816-4000
Facsimile: (703) 816-4100

Annex 1

Aim

Comparison of reactivities of core peptides I (1-20), II (37-56), III (61-80), IV (73-92) of the present invention with core peptides based on the positions (1-10), (5-20), (20-25), (35-45), (65-75) and (80-90) disclosed in Houghton document.

Method

For each of the sequences which were proposed to be immunoreactive by Houghton et al., the respective peptides were synthesized as described in the Methods section. Twenty randomly selected HCV-positive sera and 4 sera obtained from HCV-negative blood donors were taken for analysis. Assay conditions were as described in the Methods section. The Optical Density values were analysed as shown in table: 1. Furthermore, it should be made clear that the immune response to HCV is multispecific. In order to detect most of the HCV-infected cases, the use of multiple epitopes is required. Therefore, an additional reactivity of one peptide with 5% of HCV positive cases is considered as a major advantage in the screening and confirmation of HCV antibodies. An overall additional detection of 1% of HCV positive cases, or even 0.1%, or only one or a few cases out of millions of blood donations, is already considered as a very competitive advantage of the assay. In this light, the detection of only 1 additional case out of 20 HCV positive sera is considered as a major advantageous property of the particular peptide.

Results

Peptide I (Core 1-20)

Out of 20 HCV positive samples, 11 (55%) react with peptide I, and 2 samples (10%) show grey zone reactivities.

Comparison with peptide 1-10 based on the positions proposed by Houghton et al.

Samples 58, 67, 73, 75, 79, 89, 98, 99, 07, and 10, which all show positive test results on peptide I, are all negative when tested on peptide 1-10. Only one sample (5%), sample 18, is detected using the peptide 1-10. Seven samples show grey zone reactivities. Clearly peptide I contains major epitopes which are not present in peptide 1-10, allowing the detection of over half of the HCV-positive samples which is not possible using peptide 1-10.

Comparison with peptide 5-20 based on the positions proposed by Houghton et al.

Sample 07 is clearly positive using the peptide I of the invention, while it is not detected using peptide 5-20. In addition, 2 grey zone-reactive samples, 61 and 65, are clearly negative when tested on peptide 5-20. Overall, 3/20 (15%) of HCV positive sera show increased reactivity with peptide I as compared to peptide 5-20.

Peptide II (Core 37-56)

Comparison with peptides 35-45 based on the positions proposed by Houghton et al.

Out of 20 HCV positive samples, 3 (15%) react with peptide II. None of the 20 HCV-positive samples show reactivity with peptides 35-45, except for a grey zone reactivity of sample 10 with peptide 35-45. Thus, neither of these peptides is able to react with the samples 05, 98, and 18 which are positive with peptide II.

Peptide III (Core 61-80)

Out of 20 HCV positive samples, 1 (5%) is positive when tested on peptide III. Ten additional sera (50%) show borderline reactivity.

Comparison with peptide 65-75 based on the positions proposed by Houghton et al.

Sample 67 which yield as positive result when tested on peptide VI, is negative when tested on peptide 65-75. Samples 70, 79, 05, 89, 98, 17, and 18 which show grey zone reactivities when tested on peptide III, are negative when tested on peptide 65-75.

Peptide IV (Core 73-92)

Out of 20 HCV positive samples, 2 (10%) are positive using peptide IV.

Comparison with peptide 80-90 based on the positions proposed by Houghton et al.

Although proposed to be immunoreactive by Houghton et al., peptide 80-90 is completely useless for diagnostic purposes since it does not detect any of the HCV positive samples. Thus, neither of the peptide IV-positive samples showed reactivity with peptide 80-90.

The findings obtained with peptides 1-10, 20-25, 35-45, 65-75, and 80-90 which were synthesized based on the sequences proposed by Houghton et al., teach that the algorithm followed by Houghton et al. did not allow to arrive at peptides which are reactive with antibodies from HCV-positive samples. On the contrary, the proposals

of Houghton et al. Are quite misleading since e.g. peptide 45-65 also reacts with non-HCV samples.

In conclusion, from the above data, which have been generated from only a limited set of HCV-positive sera, it can already be easily deduced that each of the peptides I, II, III and IV possess unexpected reactivities as compared to the peptides suggested by Houghton et al. We therefore conclude these peptides to be inventive of the closest prior art.

Table. 1

Samples	Core 1-20	Core 37-56	Core 61-80	Core 73-92	Core HOU 1-10	Core HOU 5-20	Cor HOU 20-25	Core HOU 35-45	Core HOU 45-65	Core HOU 65-75	Core HOU 80-90
17758	543	48	39	40	38	468	34	39	38	184	44
17760	39	48	39	42	40	38	36	39	39	40	46
17761	60	48	40	42	40	39	35	39	39	47	50
17763	41	47	40	43	38	40	36	43	45	46	42
17765	51	47	41	45	40	39	36	44	41	45	49
17767	819	50	66	47	45	696	37	39	39	43	44
17770	43	52	43	50	42	43	36	48	48	39	52
17773	89	44	41	46	42	77	37	44	47	47	49
17775	71	41	46	49	46	76	39	44	48	47	53
17779	877	49	49	315	39	866	46	43	45	43	50
17783	40	50	38	50	39	47	44	40	47	48	50
17805	50	667	44	175	41	44	46	40	49	45	49
17789	1676	49	49	54	42	1473	42	39	49	41	49
17798	1160	163	45	47	47	1073	51	40	40	43	43
17799	85	44	39	55	43	59	37	41	40	50	52
17803	42	49	40	57	44	44	35	41	48	55	54
17807	228	45	48	51	48	56	46	52	555	47	48
17810	332	45	48	50	48	142	46	58	48	47	44
17817	49	49	51	52	48	46	46	49	49	39	46
17818	324	366	49	53	286	321	47	51	464	42	41
B51	48	48	50	58	50	50	41	51	40	43	51
B52	54	51	50	50	51	52	44	45	49	40	52
B53	52	48	50	51	49	51	44	51	161	43	52
B54	51	42	51	56	49	48	44	52	709	47	54